Turk J Gastroenterol *2014; 25: 730-2*

A case of uneventful ABO-incompatible liver transplantation from a deceased donor managed with routine immunosuppressive treatment

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ABSTRACT

ABO-incompatible liver transplantation (ILT) was formerly contraindicated because of the increased risk of antibody-mediated humoral graft rejection due to preformed anti-A/-B antibodies on recipient endothelial cells. A 2.5-year-old girl with end-stage liver disease underwent cadaveric donation ILT because of acute liver failure and esophageal variceal bleeding before transplantation. The patient's blood type was A Rh (–) and the donor's blood type B Rh (+). The operation and postoperative course were uneventful. The immunosuppression consisted of steroids, and tacrolimus was initiated on the day of the surgery. The patient's hemoglobin level did not change, and direct Coombs test performed daily was consistently negative. Anti-B titer was observed at a maximum of 1/8. The patient was followed up during the first year.

This case of ILT from a cadaveric donor is significant because the 2.5-year-old recipient did not experience any complications after undergoing routine immunosuppressive treatment.

Keywords: Childhood, liver transplantation, ABO-incompatible

Case Report

INTRODUCTION

Incompatible liver transplantation (ILT) was formerly contraindicated because of the increased risk of antibody-mediated humoral graft rejection due to preformed anti-A/-B antibodies on recipient endothelial cells (1). Adult ILT has long been considered a high-risk operation because the preformed antibodies against the donor's blood-type antigens have been shown to induce severe humoral rejection with a high rate of bile duct and vascular complications (2).

Egawa et al. (3) reported that these reactions would not be observed in patients under 1 year of age and that antibody production was not sufficient against blood-type antigens at this age. However, this type of intrahepatic bile duct injury has been described in children older than 1 year of age, and the intense type of liver necrosis has been observed from 8 years of age.

This report describes a case of an ILT from a cadaveric donor with routine immunosuppressive treatment in which the 2.5-year-old recipient did not present any complications.

CASE PRESENTATION

A 2.5-year-old girl, who developed end-stage liver disease of unknown etiology, underwent ILT from a cadaveric donor because of acute liver failure and esophageal variceal bleeding before the liver transplantation. The etiology of the acute liver failure could not be investigated. However, we considered the esophageal variceal hemorrhage to be secondary to end-stage liver disease or an interfering infection. End-stage liver disease was suspected on account of an increased echogenicity and rough appearance of the liver on abdominal ultrasonography, portal hypertension on portal Doppler ultrasonography, coagulation defect observed on

This case was presented at the 1st Congress of Society of Pediatrics Speciality Academy , 23-27 April 2012, Antalya, Turkey.
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Received: May 21, 2013 **Accepted:** January 26, 2014

biochemical analyses, direct hyperbilirubinemia, albumin decrease, and ascites. In an attempt to determine the etiology of her chronic liver disease, viral markers were assessed (hepatitis A, B, and C; toxoplasmosis; herpes virus; Epstein-Barr virus; and cytomegalovirus) and were found to be negative. Ceruloplasmin and 24-h urine copper values were normal. Alpha-1 antitrypsin level was also normal. Anti-nuclear antibody (-), anti-smooth muscle antibody (-), anti-liver kidney microsomal antibody (-), screening for metabolic diseases (-) and eye examinations were all normal. The patient had stage 1 encephalopathy during follow-up due to decompensated liver failure. Her condition continued to worsen, and she developed stage 2 encephalopathy immediately before transplantation.

Our patient's blood type was A Rh (–), and the donor's blood type was B Rh (+).

The operation and postoperative course were uneventful. The patient was given 10 mL/kg of A Rh (–) blood three times peri- and postoperatively. Immunosuppressive therapy consisting of steroids and tacrolimus was initiated on the day of surgery. Intravenous methylprednisolone therapy was started during surgery at 10 mg/kg, and the steroid dosage was subsequently tapered to 1 mg/kg per day at 2 weeks post-transplantation and 0.25 mg/kg per day at 6 months post-transplantation. Tacrolimus dosages were adjusted to reach trough blood levels between 10 and 15 ng/dL during the first month and between 5 and 10 ng/dL thereafter. The patient's hemogram, biochemistry, serum Anti-B titer, and direct Coombs test results were monitored daily. Her hemoglobin values did not change, but transaminase and bilirubin levels declined rapidly. Direct Coombs test results, which were monitored daily, were consistently negative. Anti-B titer was observed at a maximum of 1/8. The patient was followed-up during the first year.

Table 1. Hemogram and blood chemistry values of patient

	Before LT	After LT 2nd day	After LT 7th day	After LT 1st year
Hemoglobin (g/dL)	9.5	7.5	8.8	10.1
White cell count (/mm^3)	6090	4260	5000	7670
Platelet (/mm^3)	35000	59000	63000	369000
SGPT (IU/L)	54	326	270	14
SGOT (IU/L)	72	197	107	16
Alkaline phosphatase (IU/L)	124	298	309	87
T. Bilirubin (mg/dL)	20	3.2	2.4	0.2
D. Bilirubin (mg/dL)	8	1.8	1.1	0.1
GGT (IU/L)	220	330	472	31
Total Protein (gr/dL)	4.2	4.6	5.1	6.8
Albumin (gr/dL)	1.9	2.5	2.8	3.2
PT (sec)	31.4	11.8	11.9	12
inr	2.7	1.0	1.0	1.0
aPTT (sec)	61.9	35	22.5	25
Direct Coombs	-	-	-	-
Anti-A titer	-	-	-	-
Anti-B titer		-	1/8	-

LT: liver transplantation; SGPT: serum glutamic pyruvic transaminase; SGOT, serum glutamic oxaloacetic transaminase; GGT, gamma glutamyl transpeptidase; PT: prothrombin time; aPTT: activated partial thromboplastin time

DISCUSSION

Because it is mainly reserved for emergency rescue situations, ILT is not performed routinely (4). A number of case series on the subject have been reported, especially from Asia (5,6). Egawa et al. (3) identified two types of graft failure after ILT. They reported that acute liver necrosis occurred 1 to 2 weeks post-transplantation, while damage to the intrahepatic biliary tract developed slowly over 2 to 3 months post-transplantation. It has been suggested that these reactions do not occur in patients less than 1 year of age because antibody production against blood-type antigens is insufficient in this age group. However, cases of intrahepatic bile duct injury have been reported in children older than 1 year of age, and cases of acute liver necrosis have been reported in children from 8 years of age.

These differences in clinical presentation, which depend on the recipient's age, were reflected in the survival rates after transplantation. Five-year survival rates of recipients less than 1 year of age (infants), 1-7 years (young children), 8-15 years (children), and 16 years or older (adults) have been reported to be 76%, 68%, 53%, and 22%, respectively. Until recently, ILT in adults was contraindicated, or reserved as a last resort for emergent cases because of the extremely poor postoperative results seen in this age group (7,8).

Early preoperative desensitization, with approaches such as rituximab treatment and plasma exchange, is the key to successful ILT. A Japanese registry study reported that the incidence of antibody-mediated rejection (AMR) was significantly greater if the donor-specific anti-blood group antibody titer was more than 1/16 at the time of ILT (9). Therefore, preoperative plasma exchange should be performed, unless the original titers are 1/16 or less. Moreover, re-elevation of the titer to even more than 1/256 can occasionally occur within the first week of transplantation. In such cases, local graft infusion and/or IVIG may be a powerful tool to suppress AMR (4).

Intraportal infusion therapy, hepatic arterial infusion therapy, total plasma exchange, and quadruple immunosuppression are new therapeutic approaches for adult ILT (10,11). However, the efficacy of these approaches is yet to be demonstrated. Further, Takahashi described the AMR as single-organ disseminated intravascular coagulation (12).

Vikram et al. (13) suggested that preoperative rituximab reduced the anti-ABO antibodies sufficiently to prevent AMR, irrespective of splenectomy. In addition, they indicated that splenectomy did not seem to offer any immunological benefit in ILT when performed concomitantly with preoperative rituximab. In addition to these studies, Gelas et al. (14) suggested that ILT in small infants (<5 kg) had short- and long-term outcomes comparable to ABO-compatible grafts and that excellent results could be achieved with a standard immunosuppressive protocol.

Protocols implemented before and after transplantation in ILT cases as described in the literature were not applied in our case, and the course was uneventful after transplantation. We attribute this outcome to the liver being a tolerogenic organ and to the young age of our patient. No abnormal values were observed in our patient's hemogram and biochemical analysis, as shown in Table 1. Anti-B titer was observed at a maximum of 1/8. Therefore, plasmapheresis and other immunosuppressive treatments were not required.

We report this case to emphasize the possibility that an ILT can be performed without postoperative complications in very young children and that intensive immunosuppressive treatment is not required even if the blood type of the donor and recipient is incompatible and the recipient has decompensated liver failure.

Ethics Committee Approval: N/A.

Informed Consent: Written informed consent was obtained from patient who participated in this case.

Peer-review: Externally peer-reviewed.

Author contributions: Concept - G.T., D.Y.; Design - G.T., A.U; Supervision - H.D., A.T.A.; Resource - G.T.; Analysis&/or Interpretation - G.T., H.D., R.T.; Literature Search - G.T., D.Y.; Writing - G.T., D.Y., A.U.; Critical Reviews - R.T., H.D.

Conflict of Interest: No conflict of interest was declared by the authors.

Financial Disclosure: The authors declared that this study has received no financial support.

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